REMARKS/ARGUMENTS

Reconsideration of this application is requested. Claims 34-37, 39-46 and 57-80 and 89-94 are in the case.

I. SPECIFICATION

The disclosure is objected to because there is no brief description of the drawings. This has received attention in the present response. Withdrawal of the objection to the specification is respectfully requested.

II. THE ANTICIPATION REJECTION

Claims 34-37, 47-50, 52-55 and 77-88 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Grunenberg *et al.* (Grunenberg) for the reasons set forth in the previous Office Action. The rejection is respectfully traversed.

With conceding to the rejection, rejected claims 47-50, 52-55 and 81-88 have been canceled without prejudice. The rejection as it pertains to those claims has accordingly been rendered moot.

The invention of claim 34 is directed to crystalline moxifloxacin hydrochloride hydrate form A. This is characterized by an X-ray diffraction spectrum having the principal peaks as set forth in claim 34.

The Action asserts that presently claimed form A is anhydrous. This is not correct. Form A is not anhydrous, and paragraph [0012] of the published application specifically indicates that form A is hydrated. Claims 34-47 have been amended to specifically state this.

The hydrate nature of form A is also evident from the corresponding DSC (Figure 4) which has an endothermic peak at 73.25° C, and which corresponds to the loss of the crystallization water. Such a peak is absent from the DSC of form B (Figure 8), which is in fact anhydrous. The Turchetta declaration properly compares with the hydrated form of Grunenberg, and is thus relevant to the claimed invention.

Furthermore, attention is directed to the attached Enclosure 1 which is a comparison between the same PXRD spectrum contained in Grunenberg and that contained in the present application. As will be readily seen from the superimposed profiles, the two PXRDs differ significantly. In particular, Grunenberg's monohydrate lacks the peaks at about 7.5 2theta and 12.5 2theta (both evidenced with a double arrow). The comparison establishes that Grunenberg's monohydrate and the present hydrated form A are two different crystalline forms.

Enclosure 2 attached hereto is Brittain, *"Polymorphism of Pharmaceutical solids"*, Marcel Dekker Inc, 1999, pages 236-237. This is the **same** reference cited in the Action. This reference states that *"the identity is established if the scattering angles of the ten strongest reflections obtained for an analyte agree to within ± 0.20 degrees with that of the reference material and if the relative intensities of these reflections do not vary by more than 20%"*.

According to this criterion, the strongest reflection of form A is the peak at about 7.5 2 theta. This is missing in the diffractogram of Grunenberg's monohydrate. Consequently the basic condition for the identity of the two forms is not met.

The Action asserts that the presently claimed compound and the prior art should be compared at the same radiation parameters. Based on this, the PXRD spectrum of

Grunenberg has been compared to that of a monohydrated form crystallized from water (as in Grunenberg's Example 6) obtained under the same radiation condition of the instant compound (Enclosure 3), that is the under the conditions reported in Table 1 of the present application.

As can be seen, every peak of Grunenberg's published PXRD finds a counterpart in the experimental PXRD. The differences in the relative intensities of the peaks are due to the different preferential orientation in the samples. The two crystalline forms are thus identical. From this it follows that the use of different radiation parameters is irrelevant.

Based on the above, it is clear that the presently claimed crystalline hydrated form A is novel and different from the solid form disclosed by Grunenberg. This is irrespective of what might happen when the solid forms are in solution.

Withdrawal of the anticipation rejection is in order. Such action is respectfully requested.

III. THE OBVIOUSNESS REJECTION

Claims 34-37, 47-50, 52-55 and 77-88 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Grunenberg in view of Chemical & Engineering News, Brittain *et al.*, US Pharmacopia, Muzaffar *et al.*, Jam *et al.*, Taday *et al.* and Concise Encyclopedia Chemistry for the reasons set forth in the previous Office Action. The rejection is respectfully traversed.

Without conceding to the rejection, rejected claims 47-50, 52-55 and 81-88 have been canceled without prejudice. The rejection as it pertains to those claims has accordingly been rendered moot.

The Turchetta declaration is a proper comparison versus the closest prior art, since it compares two hydrated forms (not a hydrated *vs.* an anhydrous form). The Turchetta declaration establishes that the present hydrated form A is more soluble than the closest prior art. Furthermore, the Turchetta declaration demonstrates that the present hydrated form A retains its specific and characterizing crystalline form after compression not only with excipients but also without excipients, thus confirming that it is surprisingly stable and that it can be easily formulated into a dosage form.

The cited art does not render obvious the claimed invention. Withdrawal of the obviousness rejections is respectfully requested

IV. THE 35 U.S.C. §112, FIRST PARAGRAPH, REJECTIONS

Claims 77-88 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. Claims 47-50, 52-55 and 77-88 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement as well as failing to comply with the enablement requirement. The rejections are respectfully traversed.

As noted above, without conceding to the rejection, rejected claims 47-50, 52-55 and 81-88 have been canceled without prejudice. The formal rejections as they pertain to those claims have accordingly been rendered moot.

Referring to the remaining claims, with regard to claims 77-80, the application expressly states that moxifloxacin hydrochloride form A has workability and fluidity characteristics, which are optimal for formulation and does not lose these properties even after compression tests, as confirmed by the Turchetta declaration. Moreover, Example 6 makes specific reference to tablets. It is clear that compressed formulations, i.e. the tablets, were in the possession of the inventors when the application was filed. Withdrawal of the written description rejection is respectfully requested.

With regard to the rejection of claims 47-50, 52-55 and 77-88, rejected on written description and enablement grounds, claims 47-50, 52-55 and 81-88 have been canceled without prejudice. Claims 77-80 are enabled and described for the above-discussed reasons. Withdrawal of this rejection is respectfully requested.

V. THE 35 U.S.C. §112, SECOND PARAGRAPH, REJECTION

Claims 77-88 are rejected under 35 U.S.C. 112, second paragraph, as allegedly indefinite because it is unclear how a crystalline compound by itself can be formed and maintained in a tablet without any inert ingredients. Further, claims 85-88 fail to recite the inert excipients present in the pharmaceutical compositions.

As previously stated, the Turchetta declaration makes clear that the present hydrated form A retains its specific and characterizing crystalline form after compression with and without excipients. Nevertheless, in order to better define the scope of the claims, claims 81-88 have been cancelled without prejudice and claims 77-80 have been amended to recite "a pharmaceutical composition in the form of a tablet...."

As well known in the art, a tablet is in fact a pharmaceutical dosage form. It comprises a mixture of active substances and excipients, usually in powder form, pressed or compacted into a solid (see for instance http://en.wikipedia.org/wiki/Tablet). Consequently, the term "tablet", as recited in currently amended claims 77-80, necessarily implies that the claimed pharmaceutical composition is solid and that it contains pharmaceutically acceptable excipients in addition to crystalline moxifloxacin hydrochloride hydrate form A.

Claims 77-80 are enabled and described for the above-discussed reasons. Withdrawal of this rejection is respectfully requested.

Favorable action is awaited.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: /Leonard C. Mitchard/
Leonard C. Mitchard
Reg. No. 29,009

LCM:lff
901 North Glebe Road, 11th Floor
Arlington, VA 22203-1808
Telephone: (703) 816-4000
Facsimile: (703) 816-4100
Attachments: Enclosures 1-3